What are the Latest Treatment Advances in Parkinson disease

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Director, Functional Imaging of Neurodegenerative Disorders Lab
Overview

- Recently approved therapies
- Exciting science
- Should I participate in research?
An Aside: What Matters Most in PD…

- The Food and Drug Administration (FDA) relies on patient/family feedback to identify important areas of focus.
- FDA published “The Voice of the Patient” in April 2016
- Notable Findings:
  - Participants emphasized the frustration associated with uncertainty about their disease (e.g. onset, progression, advanced stages)
  - Participants commented on the impact of stress on their motor symptoms (e.g. tremor, freezing, etc.)
  - Participants described cognitive impairment and difficulty focusing as a major concern
  - PD impacted quality of life through reliance on others, loss of ability to work, and rise of isolation.
The findings from the “Voice of the Patient” report help to drive therapies.

The complexity of PD requires a holistic approach to the entire individual and family unit

- Fear of uncertainty ⇒ Education Initiatives and Support Groups
- Impacts of stress ⇒ Medication and non-medication (Mindfulness)
- Cognitive impairment ⇒ Recognition, Treatment and Research
- Loss of Autonomy ⇒ Physical therapies, Home care assistance programs, education, redirecting talents to new areas.

Your voice matters and helps to drive research and discovery.
Recently Approved Therapies - Nuplazid™

- Pimavanserin (Nuplazid™) received FDA approval in April 2016 for the treatment of Parkinson disease Psychosis (Hallucinations)
- Hallucinations in PD are different than those in Schizophrenia (visual vs. auditory)
- The cause of hallucinations in PD is different than the cause in Schizophrenia (cognitive impairment vs. excessive dopamine)
- Despite these major differences, PD psychosis was treated using medications intended to treat Schizophrenia.
- Unlike previously used medications, Nuplazid™ works on the serotonin receptor without blocking dopamine.
- The potential advantage is treatment of hallucinations without impacts on motor function.
Recently Approved Therapies – Infinity™ DBS

- The St. Jude Medical (now Abbott) Infinity™ DBS system received FDA approval in 2016
- Two DBS options now available:
  - Medtronic Activa™
  - St. Jude Infinity™
- Systems are quite similar, though potential pros/cons to each
- A unique possible feature of the Infinity™ system is the Directional lead
- Limited studies to date showing benefits to the directional lead
Exciting Scientific Updates – Disease Modifying

- Disease-modifying therapies refer to strategies intended to:
  - Prevent
  - Slow
  - Halt progression

- Strategies include:
  - Reducing oxidative damage or inflammation
  - Promoting neuronal support
  - Targeting abnormal proteins

<table>
<thead>
<tr>
<th>Antioxidant</th>
<th>Pre-clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>To Patients</th>
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<td>Glutathione</td>
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<td>Inosine</td>
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<th>Neurotrophic Factors</th>
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<td>GDNF</td>
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<td>CERE-120</td>
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<td>PYM 50028 (Cogane)</td>
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<th>Alpha-synuclein</th>
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<td>Affitope</td>
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<td>Phenylbutyrate</td>
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<th>Repurposed Compounds</th>
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<td>Exenatide (Byetta)</td>
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<td>Isradipine</td>
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<td>Nicoderm Patch</td>
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From MJFF
Exciting Scientific Updates – Motor

- Treatment of the cardinal motor symptoms of PD have been focused primarily on dopamine
- New strategies include:
  - Better delivery of dopamine
  - Enhanced brain production of dopamine (gene therapy)
  - Novel mechanisms to treat dyskinesias, freezing, and sudden ‘off’ periods
  - Improvement of imbalance

![Table](chart.png)

From MJFF
Exciting Scientific Updates – Non-Motor

- Treatment of the non-motor symptoms has greater impact on improvement of QOL

- Areas of current focus:
  - Constipation
  - Swallowing problems
  - Impulse control
  - Cognitive impairment

<table>
<thead>
<tr>
<th>Condition</th>
<th>Pre-clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>To Patients</th>
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<tbody>
<tr>
<td><strong>Constipation</strong></td>
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<td>Slower than normal emptying of the stomach can lead to erratic levodopa absorption and discomfort.</td>
<td>GSK962040</td>
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<td>RM-131</td>
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<td><strong>Swallowing Problems</strong></td>
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<td>A decrease in the ability to swallow normally is a non-motor symptom of Parkinson’s.</td>
<td>Tropicamide</td>
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<td><strong>Impulse Control</strong></td>
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<td>A reduction in impulse control may be a side effect of Parkinson’s medications.</td>
<td>Naltrexone</td>
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<td><strong>Cognitive Decline</strong></td>
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<td>PD patients may experience mild cognitive impairment and some may advance to dementia.</td>
<td>Atomoxetine</td>
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<td>Droxidopa</td>
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<td>SYN-120</td>
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From MJFF
Latest Scientific Updates – Vaccines

- Vaccines are potentially the most exciting development in the history of Parkinson’s research
- Vaccines are currently being developed to help target the alpha-synuclein deposits that build up in the brain and lead to the symptoms of Parkinson’s
- Vaccines help the immune system to better recognize these deposits and clear them out
- If/when vaccines are successful at reducing alpha-synuclein, this has the potential to reverse or even “C” Parkinson’s
- The race begins…
  - Biogen Phase I (Safety) trial ongoing
  - Neuropore/UCB Phase I trial ongoing
  - Prothena/Roche Phase I trial showed safety
  - AFFiRiS Phase I trial showed safety
  - Phase II trials (Efficacy) are planned
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- Vaccines help the immune system to better recognize these deposits and clear them out.
- If/when vaccines are successful at reducing alpha-synuclein, this has the potential to reverse or even “C” Parkinson’s.
- The race begins…
  - Biogen Phase I (Safety) trial ongoing with ongoing active recruitment.
  - Neuropore/UCB Phase I trial ongoing was successful, Phase II being planned.
  - Prothena/Roche Phase Ib trial showed safety and reduced levels (up to 97%) of synuclein in the blood. Phase II starting in 2017.
  - AFFiRiS Phase Ib trial showed safety and activation of an immune response in 19 of 22 (86%) of subjects. Exploratory analyses showed that 8 of the responders did not require increased dopamine for a period of up to 3 years.
  - Phase II trials (Efficacy) are intended coming in 2017…
Latest Scientific Updates – Tasigna (Nilotinib)

- Nilotinib is an FDA-approved medication for Leukemia from Novartis
- Phase I trial of 12 patients with PD (open label…no placebo) at Georgetown showed positive findings
  - Spinal fluid testing showed reductions in toxic proteins found in PD, suggesting that they were being cleared
  - 10 of 12 patients showed ‘meaningful’ clinical improvement (reduced falls, improved cognition, improvement motor function, reduced constipation, reduced need for dopamine, etc.)
- Phase II clinical trial slight delays...stay tuned!
Latest Scientific Updates – Stem Cells

- Not new…
- Provides the potential to provide continuous endogenous dopamine
- Doesn’t treat the non-dopamine symptoms
- Doesn’t reverse the disease progression
- Many snake oil salesmen abound…
- If interested, encouraged to participate in a formal trial (for free)
  - International Stem Cell Corp (ISCO) is conducting a Phase I clinical trial in moderate to severe PD in Melbourne, Australia
# Latest Scientific Updates – Stem Cells

- **ClinicalTrials.gov**

- **Current trials:**

<table>
<thead>
<tr>
<th>Trial ID</th>
<th>Status</th>
<th>Description</th>
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<tr>
<td>1</td>
<td>Suspended</td>
<td>Autologous Mesenchymal Stem Cell Transplant for Parkinson’s Disease</td>
<td>Parkinson’s Disease</td>
<td>Procedure: Autologous Bone marrow derived stem cells transplant</td>
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<td>Mesenchymal Stem Cells Transplantation to Patients With Parkinson’s Disease</td>
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<td>Biological: bone marrow derived mesenchymal stem cells</td>
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<td>Allogeneic Bone Marrow-Derived Mesenchymal Stem Cell Therapy for Idiopathic Parkinson’s Disease</td>
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<td>Biological: Allogeneic bone marrow-derived MSCs</td>
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<td>4</td>
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<td>Parkinsonian Brain Repair Using Human Stem Cells</td>
<td>Idiopathic Parkinson Disease</td>
<td>Drug: Human Stem Cells</td>
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<td>5</td>
<td>Enrolling by Invitation</td>
<td>Molecular Analysis of Human Neural Stem Cells</td>
<td>Parkinson’s Disease; Parkinsonism</td>
<td>Procedure: Harvesting of neural stem cells</td>
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<td>6</td>
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<td>Using [18F]FDOPA PET/CT to Monitor the Effectiveness of Fetal Dopaminergic Grafts in Parkinson Disease Patients</td>
<td>Parkinson’s Disease</td>
<td>Drug: [18F]FDOPA PET/CT</td>
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<td>7</td>
<td>Recruiting</td>
<td>Study to Assess the Safety and Effects of Autologous Adipose-Derived SVF Cells in Patients With Parkinson’s Disease</td>
<td>Parkinson’s Disease</td>
<td>Procedure: Harvesting and Implantation of Adipose-Derived Stem Cells</td>
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<td>8</td>
<td>Unknown</td>
<td>Rajaviti Neuronal Adult Stem Cells Project</td>
<td>Alzheimer’s Disease; Parkinson’s Disease; Multiple Sclerosis</td>
<td>Other: Progenitor Stem Cell Culture</td>
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<td>9</td>
<td>Recruiting</td>
<td>A Study to Evaluate the Safety of Neural Stem Cells in Patients With Parkinson’s Disease</td>
<td>Parkinson Disease</td>
<td>Biological: ISC-hpNSC</td>
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<td>10</td>
<td>Recruiting</td>
<td>Outcomes Data of Adipose Stem Cells to Treat Parkinson’s Disease</td>
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Desperate patients and false hope: a troubling trend for stem cell-based therapies

JUNE 4, 2015 / TODD DUBNICOFF

A gambler’s odds are usually stacked against them but the possibility, however slim, of hitting the jackpot keeps bringing them back to the table. Now imagine, unbeknownst to them, the system is rigged so there’s a zero percent chance of any winnings. They’d essentially be giving their money away based on a false hope. Sadly, many desperate people looking for stem cell cures do exactly that.

Earlier this week, Cristin Severance, a Team10 TV news reporter in San Diego, investigated local stem cell clinics promising treatments for a number of chronic incurable diseases. Severance cites Stemgenex of La Jolla, which offers people with Parkinson’s disease the chance of improving their symptoms through a therapy using stem cells from their own fat. This opportunity comes at a cost – $15,000. According to stem cell expert Jeanne Loring of The Scripps Research Institute, there’s no prospect the treatment will work.
Local Trials at UCSD

- Multiple ongoing trials ranging from observational to therapeutic…
- Currently Enrolling:
  - SURE-PD Study - Inosine for early PD (Disease-modifying)
  - New Dopamine Agonist Study for PD with fluctuations (Motor)
  - SYNAPSE – SYN-120 medications for cognitive impairment in PD (Non-motor)
  - Cognitive rehabilitation study (Non-motor)
  - T-cell biomarker for autoimmunity in PD (Observational)
- Numerous upcoming trials, including anti-Synuclein antibodies

To learn more, call 858-822-MOVE or go to: http://movementdisorders.ucsd.edu
Thank You

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